

In the Application of:
Tirrell et al.
09/620,691
July 20, 2000

Page 2

I. AMENDMENTS

In the Claims:

Please cancel claim 2 without prejudice.
Please amend claims 1, 3 and 4.
Please add new claims 15-24.

1. (Currently Amended) An isolated A polypeptide with increased stability, relative to its corresponding wild type protein, having comprising at least one non-natural amino acid incorporated inserted into a hydrophobic region of the wild-type polypeptide, wherein the non-natural amino acid causes an increase in the thermal stability of the polypeptide as compared with a corresponding wild type polypeptide not having the non-natural amino acid amino acid so replaced is leucine, isoleucine, or valine.

2. (Cancelled)

3. (Currently Amended) The isolated polypeptide non-natural amino acid of claim 1, wherein the non-natural amino acid is different from its corresponding natural amino acid in side chain functionality a hydrophobic non-natural amino acid.

4. (Currently Amended) The isolated polypeptide of claim 1, wherein the non-natural amino acid is a hydrophobic non-natural amino acid selected from the group consisting of an unsaturated hydrophobic amino acid; a fluorinated hydrophobic amino acid; 2-amino-3-methyl-4-pentenoic acid; 5,5,5-trifluoroleucine; 5,5,5,5',5',5'-hexafluoroleucine; 2-amino-3,3,3-trifluoro-methylpentanoic acid; 2-amino-3-methyl-5,5,5-trifluoropentanoic acid; 2-amino-3-methyl-4-pentenoic acid; 4,4,4-trifluorovaline; 4,4,4,4',4',4'-hexafluorovalin; 4,4,4,4',4',4'-hexafluorovaline; homoallylglycine; homoproparglycine; and p-fluorophenylalanine.

In the Application of:
Tirrell et al.
09/620,691
July 20, 2000

Page 3

5-14. (Withdrawn)

Please add the following new claims:

--15. (New) The isolated polypeptide of claim 3, wherein the non-natural amino acid is a hyper-hydrophobic amino acid.

16. (New) The isolated polypeptide of claim 1, wherein the hydrophobic region of the polypeptide contains at least one leucine, isoleucine, or valine.

17. (New) The isolated polypeptide of claim 1, wherein the hydrophobic region of the polypeptide contains at least one methionine or phenylalanine.

18. (New) The isolated polypeptide of claim 1, wherein the non-natural amino acid is inserted at a site adjacent to leucine, isoleucine, or valine in the hydrophobic region of the polypeptide.

19. (New) The isolated polypeptide of claim 1, wherein the non-natural amino acid is inserted at a site adjacent to methionine or phenylalanine in the hydrophobic region of the polypeptide.

20. (New) The isolated polypeptide of claim 1, wherein the polypeptide contains at least one α -helical structure.

21. (New) The isolated polypeptide of claim 1, wherein the polypeptide is a cytokine, membrane protein or an enzyme.

22. (New) The isolated polypeptide of claim 1, wherein the polypeptide is a tumor necrosis factor, granulocyte colony stimulating factor, erythropoitin, subtilisin, thermolysin, dehydrogenase, or esterase.

In the Application of:
Tirrell et al.
09/620,691
July 20, 2000

Page 4

23. (New) The isolated polypeptide of claim 1, wherein the non-natural amino acid is a fluorinated amino acid.

24. (New) The isolated polypeptide of claim 1, wherein the polypeptide is a leucine zipper or coiled-coil protein. --